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Readmissions and costs in cadaveric and living-donor lobar lung transplantation: Analysis using a national database

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Living-donor lobar lung transplantation (LDLLT) is a well-established surgical procedure with favorable outcomes; however, the frequency of readmission and costs in LDLLT are poorly understood. Here, we aimed to compare health care costs and readmissions at 90 days and 1 year after the index discharge in LDLLT and cadaveric lung transplantation (CLT) and evaluate the reasons for readmission and in-hospital mortality. In this retrospective cohort study, we used the Diagnosis Procedure Combination database, a nationwide inpatient database in Japan to obtain initial lung transplantation data for all patients from July 2010 to March 2020. Multivariable Poisson or multiple regression analyses after multiple imputation was performed to compare the cumulative number of readmissions and costs between patients receiving LDLLT and CLT. Among 514 recipients, 115 (22%) underwent LDLLT and 399 (78%) received CLT. Overall, in-hospital mortality after transplantation was 4.5%. The LDLLT group showed a significantly lower crude readmission rate (90 days, 22% vs 37%, $p = 0.004$; 1 year, 48% vs 62%, $p = 0.031$) and median readmission cost (90 days, United States dollar (USD) 0 vs 0, $p = 0.003$; 1 year, USD 1178 vs 4714, $p = 0.005$) than the CLT group. Multivariable regression analyses showed that the LDLLT group had a lower risk of readmission (incidence rate ratio, 0.59; 95% confidence interval, 0.38-0.92; $p = 0.020$) and lower costs at 90 days (difference, USD −11,629; 95% confidence interval, −5682 to −17,462; $p < 0.001$). The most frequent cause of readmission was pneumonia in both groups. LDLLT was associated with lower readmissions and health care costs in comparison with CLT. Our findings provide a scientific basis for further studies with larger cohorts.
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Lung transplantation is the definitive treatment for end-stage lung failure, and living-donor lobar lung transplantation (LDLLT) has emerged as an alternative to cadaveric lung transplantation (CLT) to alleviate the problems associated with donor shortage.[1-3] Despite the 3-fold increase in the number of CLTs after the amendment of the Japanese Organ Transplant Law in 2010,[4-6] LDLLT is still performed in approximately 20% of patients in Japan because of ongoing donor shortages.[4,5]

After the first successful LDLLT,[1,7] similar survival rates were reported for LDLLT and CLT,[3,4] with patient survival up to 90% in the first year.[3,4,8,9] However, long-term outcomes have not improved much in the past decade.[10] The main causes of mortality are related to the nature of transplanted lungs, which can easily cause complications such as infections or chronic lung allograft dysfunction under immunosuppression.[11-13] Chronic lung allograft dysfunction, including bronchiolitis obliterans syndrome, remains the main challenge after lung transplantation[12,13] because it can necessitate readmission for treatment. The readmission rate for recipients who underwent CLT in the United States is reported to be approximately 75% in the first year,[14,15] which reflects a substantial financial burden in health care. Although LDLLT is expected to lead to fewer readmissions owing to postoperative complications because of its short ischemic time, mild primary graft dysfunction, and favorable immunologic compatibility,[3] the frequency of readmission and costs after LDLLT have rarely been investigated.

In this study, we investigated the frequency of readmission and costs in lung transplantation using a nationwide inpatient database in Japan. We hypothesized that LDLLT may be associated with lower costs of readmission after discharge than CLT. Our results will help clarify index admission and readmission costs in Japan. Further, our study will provide a scientific basis for further studies with larger cohorts.

Materials and methods

Data collection

This nationwide retrospective cohort study was conducted using the Diagnosis Procedure Combination database, a national inpatient database in Japan. The discharge abstracts and administrative claim records in the database were obtained from approximately 1200 acute care hospitals, which included all transplant centers.[16] Discharge abstracts were recorded by the attending physicians at discharge for each patient. The database contained detailed information on patients' age, sex, body mass index, activities of daily living (Barthel index), smoking status, medication, interventional procedure, anesthesia, surgical procedure, and discharge status. The database also included the primary diagnosis, comorbidities on admission, and complications during hospitalization; all data were recorded using International Classification of Diseases, 10th Revision (ICD-10) codes. Inpatient hospital costs for each patient were calculated from the administrative claim records and included the costs of consultations, hospitalization, pharmaceuticals, procedures, radiology (medical imaging), surgery and anesthesia, clinical examination (blood testing), and other costs. Medical costs for donors were not included in the claims. We used a conversion rate of 100 Japanese yen to 1 United States dollar (USD). Reasons for readmission were determined using the primary and admission-precipitating diagnoses in the database.[16]

The Ethics Committee and Institutional Review Board of the University of Tokyo approved the study protocol (approved number: 3501-5, date: May 3, 2021). Given the anonymous nature of the data, the need for informed consent from individuals was waived.

Identification of patients

We identified patients who underwent lung transplantation for the first time from July 1, 2010, to March 31, 2020, and excluded patients who were admitted for retransplantation or combined living-lobar and cadaveric lung transplantation (known as hybrid lung transplantation). The remaining patients who were eligible for further analyses were categorized into CLT and LDLLT groups (Figure 1) according to the type of lung transplantation.

Covariates

We categorized the patients' aged < 30, 30 to 44, and ≥45 years into 3 groups. Body mass index was categorized as < 18.5 or ≥18.5 kg/m^2. Activities of daily living on admission were assessed using the Barthel index (range, 0-100), which was categorized as 0-90 and 95-100.[17] Patients with missing data were categorized into the group with missing data. Underlying diseases and comorbidities were identified using the ICD-10 codes (Table S1). Perioperative blood transfusion and procedures in the intensive care unit (ICU) were also examined. These procedures included cardiopulmonary bypass, extracorporeal membrane oxygenation, nitric oxide inhalation, mechanical ventilation, tracheal intubation, high-flow nasal cannula therapy, non-invasive positive pressure ventilation, tracheotomy, plasmapheresis, continuous hemodiafiltration, epidural analgesia, cardiac catheterization, pulmonary function tests, and removal of hematoma.

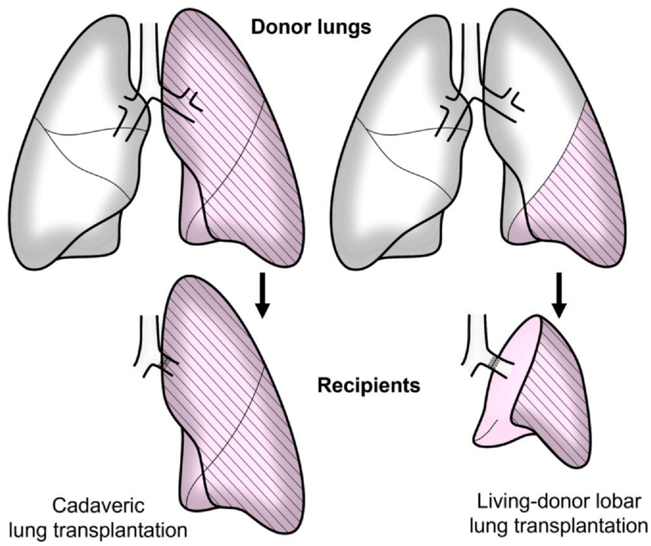

Figure 1 Types of lung transplantation. In both types of single-lung transplantation, the organs are donated by 1 donor, as shown in the above figure. For bilateral lung transplantation, 2 donors are required in living-donor lobar lung transplantation, unlike cadaveric lung transplantation.

Outcomes

The primary study outcome was the frequency of readmission at 90 days and 1 year after the index discharge for the first lung transplantation among patients who underwent CLT or LDLLT. The secondary outcome was the total medical costs for the index hospitalization and readmissions. We also examined the reasons for rehospitalization and all-cause mortality within 90 days and 1 year after lung transplantation.

Statistical analysis

Numerical variables were expressed as mean (standard deviation) or median (interquartile range [IQR]). Student *t*-test or Mann-Whitney U test was used to compare numerical variables between the 2 groups, as appropriate. All categorical variables were expressed as number and percentage and were compared using the chi-square or Fisher's exact test, as appropriate. Multiple imputation was used to account for missing values in 4 variables[18]: body mass index, Barthel index, smoking status, and the use of inhaled nitric oxide in the ICU. Additional details on multiple imputation by chained equations are described in online Data S1. We then compared the number of readmissions between the CLT and LDLLT groups by using multivariable Poisson regression models with generalized estimating equations to account for within-hospital clustering. We applied cluster-robust standard errors for adjustment of clustering. Incidence rate ratios (IRRs) are presented with 95% confidential intervals (CIs) for the Poisson regression model. Medical costs at 90 days and 1 year after the index hospitalization were compared with multiple regression models using the log-link function with generalized estimating equations. Intergroup differences in costs are presented with 95% CIs in the multiple regression models. We also assessed all-cause mortality at 90 days and 1 year after the index hospitalization in the 2 groups. The following variables were adjusted in all regression models: sex, body mass index, Barthel index, age, smoking status, surgical procedure, interstitial lung disease, pulmonary arterial hypertension, rejection, diabetes mellitus, chronic heart failure, tracheostomy, length of stay, inhaled nitric oxide use in the ICU, and medical costs. These variables were chosen because they were deemed clinically significant and potential confounders. To validate the results, we conducted a sensitivity analysis using a matched-pair cohort (online Data S1). A 2-sided p-value <0.05 was considered statistically significant. All analyses were performed using Stata version 17 (StataCorp LLC, College Station, TX).

Results

Among 520 patients who underwent lung transplantation during the 10-year study period, we excluded 4 patients who had undergone retransplantation and 2 who underwent hybrid lung transplantation. Thus, we included 514 eligible patients (399 in the CLT group and 115 in the LDLLT group Figure 2). During the study period, a total of 9 hospitals conducted lung transplants. Out of these, 7 facilities performed both CLT and LDLLT procedures.

Patient characteristics at lung transplantation

The mean (standard deviation) age of patients was 41 (16) years, and 49% of the patients in the overall cohort were women (Table 1). The mean age in the LDLLT group was significantly lower than that in the CLT group. The proportion of patients aged <30e years in the LDLLT group was 62%. Body mass index and the proportion of patients with a history of smoking were lower in the LDLLT group. Interstitial lung disease was the most common diagnosis in patients who underwent lung transplantation. There were no cases of extracorporeal membrane oxygenation (ECMO) bridge to lung transplant, and a total of 46 patients required mechanical ventilation prior to surgery (16 for CLT and 30 for LDLLT).

Surgery and postoperative course before discharge

Overall, 45% of patients underwent bilateral lung transplantation (Table 2). The proportion of patients receiving cardiopulmonary support was higher in the LDLLT group than in the CLT group (71% vs 41%, $p < 0.001$). The median (IQR) intubation period was 11 (4-27) days and the median (IQR) length of ICU stay was 14 (9-14) days. All patients received postoperative triple-drug immunosuppression therapy with

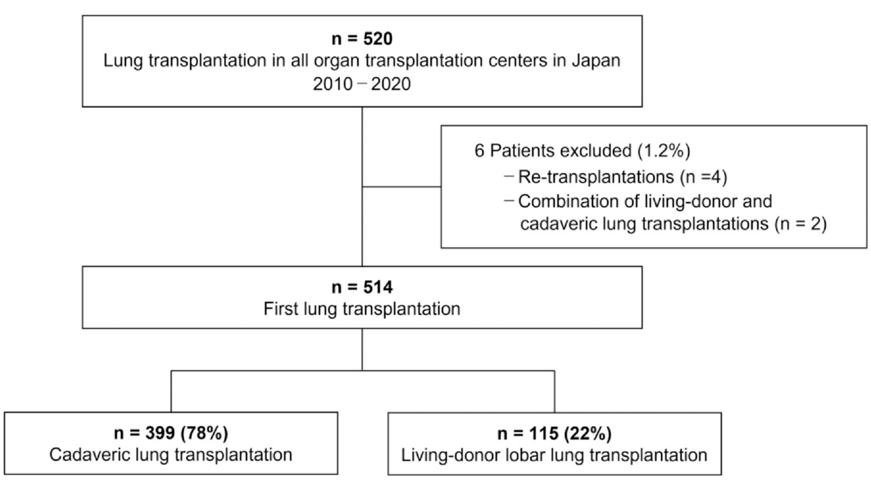

Figure 2 Patient flowchart. After excluding retransplantations and special procedures, 514 recipients who underwent standard lung transplantation for the first time were included in the study.

Table 1 Recipient Characteristics at Admission for Lung Transplantation

	Overall study population (*n* = 514)	CLT (*n* = 399)	LDLLT (*n* = 115)	*p*-value
Age (years)				< 0.001
< 30	138 (27)	67 (17)	71 (62)	
30–44	117 (23)	104 (26)	13 (11)	
≥45	259 (50)	228 (57)	31 (27)	
Female sex	254 (49)	201 (50)	53 (46)	0.418
Body mass index (kg/m^2)				< 0.001
< 18.5	276 (54)	194 (49)	82 (71)	
≥18.5	236 (46)	203 (51)	33 (29)	
Missing	2 (0.4)	2 (0.5)	0 (0)	
Barthel index				0.005
95-100	189 (36)	153 (38)	36 (31)	
0-90	234 (46)	187 (47)	47 (41)	
Missing	91 (18)	59 (15)	32 (28)	
Former and current smoker	144 (28)	128 (32)	16 (14)	< 0.001
Causes of transplantation				
Interstitial lung disease	169 (33)	126 (32)	43 (37)	0.242
COPD/emphysema[a]	93 (18)	65 (16)	28 (24)	0.048
PAH	61 (12)	49 (12)	12 (10)	0.590
Bronchiolitis obliterans[a]/diffuse panbronchiolitis[a]	63 (12)	36 (9)	27 (23)	< 0.001
LAM	54 (11)	54 (14)	0 (0)	< 0.001
Graft-vs-host disease	30 (6)	13 (3)	17 (15)	< 0.001
Bronchiectasis	18 (4)	18 (5)	0 (0)	< 0.001
Rejection	12 (2)	7 (2)	5 (4)	0.105
Cystic fibrosis	5 (1)	2 (1)	3 (3)	0.042
Sarcoidosis	2 (0.4)	2 (1)	0 (0)	0.449
Comorbidities				
Diabetes mellitus	22 (4)	16 (4)	6 (5)	0.874
Chronic heart failure	27 (5)	21 (5)	6 (5)	0.985
Hypertension	6 (1)	4 (1)	2 (2)	0.517

Abbreviations: CLT, cadaveric lung transplantation; COPD, chronic obstructive pulmonary disease; LAM, lymphangioleiomyomatosis; LDLLT, living-donor lobar lung transplantation; PAH, pulmonary arterial hypertension.

Data are presented as *n (%) unless otherwise indicated.*

[a]Noted that some patients may be duplicated because the same ICD-10 code encompasses 3 different disease groups. Therefore, the total number of cases for the cause of transplantation does not match in each group.

cyclosporine or tacrolimus, azathioprine or mycophenolate mofetil, and corticosteroids. Approximately 15% of patients underwent an emergent operation for postoperative hemorrhage, and the proportions were similar between the 2 groups. Patients in the LDLLT group were more likely to receive blood transfusion. The median (IQR) length of stay in the hospital was 76 days (58-107). In-hospital mortality after CLT and LDLLT was 4% (17/399) and 5% (6/115), respectively.

Readmission to an acute care hospital and all-cause mortality after index hospitalization

After excluding 23 patients (4.5%) who died in the hospital at the first lung transplantation (Table 2), the remaining 491 patients were eligible for analyses of readmission. Of these, 164 patients (33%) were admitted within 90 days after discharge, for a total of 222 hospitalizations (median, 1; range, 1-7 hospitalizations). The 90-day readmission rate was 37% (140/382) in the CLT group and 22% (24/109) in the LDLLT group (Figure 3). Within 1 year after discharge, 291 patients (59%) were readmitted, with a total of 710 hospitalizations (median, 2; range 1-20 hospitalizations). The 1-year readmission rate was 62% (236/382) in the CLT group and 48% (55/109) in the LDLLT group. Crude 90-day and 1-year readmission rates were both significantly lower after LDLLT ($p = 0.004$ and $p = 0.031$, respectively). Fewer patients had multiple readmissions (≥2 hospitalizations) at 90 days and 1 year in the LDLLT group ($p = 0.164$ and $p = 0.0002$, respectively). In the multivariable Poisson regression analysis, the LDLLT group still showed a significantly lower risk of frequent readmissions within 90 days (IRR, 0.59; 95% CI, 0.38-0.92; $p = 0.020$; Table 3), while the 2 groups showed no significant difference for readmissions within 1 year after discharge (IRR, 0.65; 95% CI, 0.37–1.12; $p = 0.149$). The 90-day and 1-year mortality

Table 2 Surgery and Management During Hospitalization

	Overall study population ($n = 514$)	CLT ($n = 399$)	LDLLT ($n = 115$)	p-value
Operative year				0.002
2010-2013	84 (16)	57 (14)	27 (23)	
2014-2016	189 (37)	139 (35)	50 (43)	
2017-2020	241 (47)	203 (51)	38 (33)	
Surgical procedure				< 0.001
Bilateral LTx	230 (45)	151 (38)	79 (69)	
Single LTx	284 (55)	248 (62)	36 (31)	
CPB/ECMO	245 (48)	163 (41)	82 (71)	< 0.001
Inhaled nitric oxide	71 (14)	66 (17)	5 (4)	0.001
Mechanical ventilation	481 (94)	369 (92)	112 (97)	0.058
Tracheal intubation,[a] days	11 [4-27]	10 [4-26]	15.5 [5-29]	0.035
High-flow nasal cannula therapy	41 (8)	33 (8)	8 (7)	0.647
Non-invasive positive pressure ventilation	14 (3)	8 (2)	6 (5)	0.062
Tracheotomy	211 (41)	162 (41)	49 (43)	0.700
Plasmapheresis	25 (5)	20 (5)	5 (4)	0.770
Continuous hemodiafiltration	43 (8)	34 (9)	9 (8)	0.812
Epidural analgesia	100 (19)	86 (22)	14 (12)	0.025
Cardiac catheterization	56 (11)	41 (10)	15 (13)	0.401
Pulmonary function tests	283 (55)	223 (56)	60 (52)	0.480
Transfusion	473 (92)	358 (90)	115 (100)	< 0.001
Removal of hematoma	77 (15)	61 (15)	16 (14)	0.716
ICU stay,[a] days	14 [9-14]	14 [9-14]	14 [10-14]	0.106
Hospital stay,[a] days	70 [53-94]	70 [53-98]	69 [54-9]	0.491
All-cause in-hospital mortality[a]	23 (5)	17 (4)	6 (5)	0.662

Abbreviations: CLT, cadaveric lung transplantation; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; LDLLT, living-donor lobar lung transplantation; LTx, lung transplantation.

Data are presented as *n (%) or median with interquartile range, unless otherwise indicated.*

[a]Mann-Whitney U test.

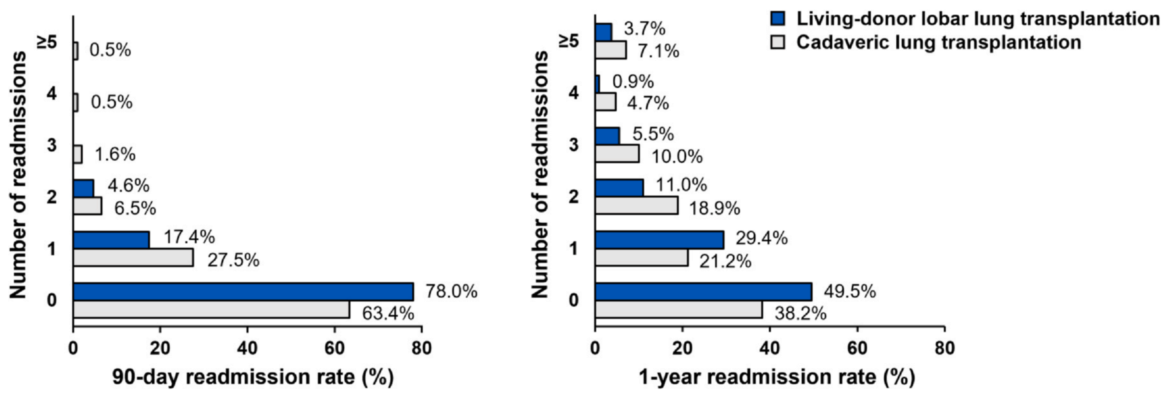

Figure 3 Number of readmissions after discharge from the first lung transplantation. The blue bar shows the readmission rates in living-donor lobar lung transplantation; the gray bar shows the readmission rates in cadaveric lung transplantation.

after discharge from the index hospitalization were, respectively, 2.1% (8/382) and 4.7% (18/382) in the CLT group and 3.7% (4/109) and 5.5% (6/109) in the LDLLT group, with no significant intergroup difference (90 days, $p = 0.312$; 1 year, $p = 0.735$).

Medical costs associated with initial admission and subsequent readmissions

Median total costs of lung transplantation were USD 108,286 (IQR 87,050-146,246), of which approximately 42% was the cost of surgery, including anesthesia. The total cost of hospitalization for LDLLT was significantly lower than that for CLT (median: USD 96,280 vs 111,447; $p = 0.008$; Table 4). Total medical costs for hospitalization within 90 days and 1 year after discharge were both lower in the LDLLT group ($p = 0.003$ and $p = 0.005$, respectively; note that patients who were not hospitalized during these periods were included; Table 4). With the multiple regression models, the medical costs within 90 days after the index hospitalization were significantly lower in the LDLLT group (difference: USD −11,629; 95% CI, −5682

Table 3 Estimation of the Cumulative Number of Readmissions After Lung Transplantation (After Multiple Imputation) Using a Multivariable Poisson Regression Model With Generalized Estimating Equations

Readmission	CLT	LDLLT	Adjusted IRR	95% CI	*p*-value
90 days	140 (35)	24 (21)	0.596	0.388–0.916	0.018
1 year	236 (59)	55 (48)	0.647	0.372–1.123	0.122

Abbreviations: CI, confidence interval; CLT, cadaveric lung transplantation; ICU, intensive care unit; IRR, incidence rate ratio; LDLLT, living-donor lobar lung transplantation.

The following covariates were used for adjustment: sex, body mass index, Barthel index, age, smoking status, surgical procedure, interstitial lung disease, pulmonary arterial hypertension, rejection, diabetes mellitus, chronic heart failure, tracheostomy, length of stay, inhaled nitric oxide use in the ICU, and medical costs.

to −17,462, $p < 0.001$; Table 5), while the medical costs at 1 year after the index hospitalization did not differ significantly between the 2 types of lung transplant (difference: USD −8220; 95% CI, −6374 to 22,773; $p = 0.271$).

Reasons for readmission

Table S2 shows the main reasons for readmission within 1 year after discharge. Pneumonia was the most frequently recorded diagnosis at readmission, followed by bronchiolitis obliterans. The 2 groups showed no significant differences in the incidence of pneumonia or bronchiolitis obliterans.

Validation by matched-pair cohort

Tables S3 and S4 show a sensitivity analysis conducted using a matched-pair cohort. Eighty-six pairs were matched between the CLT and the LDLLT groups. The 2 groups were well matched for 7 baseline characteristics. In the cohort, a significant difference between the 2 groups persisted, specifically in the area of medical costs within the first 90 days following the index hospitalization ($p = 0.021$).

Discussion

Using a nationwide inpatient database in Japan, we examined the readmission rates and total medical costs after the index hospitalization for LDLLT and CLT. In comparison with the CLT group, the LDLLT group showed a lower rate of rehospitalization, fewer readmissions within 90 days after discharge, and lower total costs for hospitalization. Similar trends were observed 1 year after discharge, although with no significant differences. These results support our hypothesis that LDLLT may be more beneficial than CLT in terms of recipients' postoperative conditions and health care costs.

Short-term survival after lung transplantation has improved with advances in postoperative management and immunosuppressive drugs.[19,20] In our study, the 1-year survival rate was 91% from 2010 to 2020, which is comparable to the > 85% survival rate reported in other countries.[3,4,8,9] The CLT and LDLLT groups showed no significant difference in survival. Our outcomes for both surgical types were consistent with the findings of a Japanese national report in 2013.[4] Despite the absence of differences in survival between the 2 groups, LDLLT recipients used acute care services less often than CLT recipients after discharge.

Lung transplantation is associated with the highest readmission rate among all types of solid organ transplant, except intestinal transplantation.[8] The readmission rate within 90-days and 1-year post-CLT discharge in the United States was 44%-52% and 65%-84%,[14,15,21] respectively, and the corresponding rates in our study were comparable (37% and 62%, respectively). The rates of rehospitalization after LDLLT were 22% at 90 days and 48% at 1 year, which were lower than those after CLT. Japan has maintained its universal health care coverage system for over 60 years.[22] Unlike Medicare or Medicaid in the United States, the Japanese health care coverage system does not have age restrictions, is not limited to specific diseases, and has no limits on enrollment according to patients' income.[8,22-24] Both physicians and recipients are therefore less likely to hesitate to readmit a patient under a system where all patients are equally supported by health insurance for medical care. These factors ensured the comparability of readmission rates after discharge between CLT and LDLLT while indicating that the lower rate of readmission after LDLLT can be attributed to differences in the incidence of postdischarge complications requiring hospitalization.

In our study, pneumonia was the most-inferred cause of readmission after lung transplantation. Previous studies have also reported pneumonia, infections, and airway complications as the most frequent diagnoses at readmission.[8,15,16,25] However, 14% of recipients after discharge developed pneumonia in our study, which was lower than the 25% reported in a previous study.[15] The difference between our study and previous studies in the USA may be partially explained by differences in the length of hospital stay after lung transplantation and in the discharge criteria. The hospital stay for lung transplantation is approximately 3 weeks in the United States,[10,14,15] whereas patients in our study were hospitalized for approximately 2 months. Transplant centers in Japan provide physical and pulmonary rehabilitation for both CLT and LDLLT patients to promote postoperative recovery during hospitalization rather than transferring patients to a rehabilitation facility. Additionally, the use of standard indications for discharge in transplant recipients may have reduced the risk of aspiration and stabilized activities of daily living. Therefore, the discharge criteria very likely contributed to a decreased incidence of pulmonary infection.

Table 4 Medical Costs at Index Admission and Readmissions

	Index admission			90 days after index discharge[a]			1 year after index discharge[a]		
	CLT ($n = 399$)	LDLLT ($n = 115$)	p-value	CLT ($n = 382$)	LDLLT ($n = 109$)	p-value	CLT ($n = 382$)	LDLLT ($n = 109$)	p-value
Consultations	1271 [983-1481]	1338 [1043-1548]	0.164	0 [0-86]	0 [0-0]	0.014	85 [0–350]	0 [0-132]	0.007
Hospital fee	24,324 [19,388-31,135]	27,253 [22,883-32,419]	0.010	0 [0-2443]	0 [0-0]	0.003	2342 [0-8197]	596 [0-3870]	0.012
Injection (medication)	17,835 [11,787-26,824]	17,048 [11,996-28,979]	0.582	0 [0-24]	0 [0-0]	0.013	12 [0-902]	0 [0-466]	0.089
Oral drug (medication)	3631 [1689-6828]	1890 [1401-3021]	< 0.001	0 [0-219]	0 [0-0]	0.002	123 [0-1113]	0 [0-301]	0.002
Other	1271 [881-1927]	1515 [1079-2105]	0.020	0 [0-0]	0 [0-0]	0.149	0 [0-187]	0 [0-50]	0.058
Procedure	2460 [1240-5807]	2855 [1612-5052]	0.323	0 [0-0]	0 [0-0]	0.009	0 [0-41]	0 [0-20]	0.070
Radiology	2004 [1461-2772]	2328 [1764-3098]	0.002	0 [0-330]	0 [0-0]	0.004	340 [0-1349]	0 [0-823]	0.005
Surgery and anesthesia	51,166 [39,336-66,771]	35,825 [29,439-46,495]	< 0.001	0 [0-0]	0 [0-0]	0.048	0 [0-110]	0 [0-0]	0.003
Test	3665 [2322-5718]	4358 [2893-6473]	0.016	0 [0-578]	0 [0-0]	< 0.001	626 [0-2218]	0 [0-1014]	< 0.001
Total costs (USD)	111,447 [88,800-148,659]	96,280 [83,571-133,864]	0.008	0 [0-5197]	0 [0-0]	0.003	4714 [0-17,904]	1178 [0-6220]	0.005

Abbreviations: CLT, cadaveric lung transplantation; LDLLT, living-donor lobar lung transplantation.
Data are presented as median with interquartile range.
Mann-Whitney U test was used to compare the CLT and LDLLT groups.
[a]Patients who were not hospitalized during these periods were included.

Table 5 Estimation of Total Costs Including Index Admission and Readmissions in LDLLT in Comparison with CLT (After Multiple Imputation) Using a Multiple Regression Model With Generalized Estimating Equations

	CLT	LDLLT	Adjusted coefficient	95% CI	*p*-value
90 days after index admission	114,348 [92,719-151,660]	101,190 [83,978-135,353]	−11,629	−5682 to −17,462	< 0.001
1 year after index admission	122,878 [98,033-170,994]	108,381 [87,882-144,584]	−8220	−6374 to −22,773	0.271

Abbreviations: CI, confidence interval; CLT, cadaveric lung transplantation; ICU, intensive care unit; LDLLT, living-donor lobar lung transplantation.. Medical costs in USD.

The following covariates were used for adjustment: sex, body mass index, Barthel index, age, smoking status, surgical procedure, interstitial lung disease, pulmonary arterial hypertension, rejection, diabetes mellitus, chronic heart failure, tracheostomy, length of stay, inhaled nitric oxide use at ICU, and medical costs.

Medical costs for the index admission and later readmissions were significantly lower in the LDLLT group than in the CLT group. The LDLLT group also showed significantly lower total costs at 90 days after the index hospitalization and fewer readmissions. The reported cost estimates across countries vary depending on the nature of insurance coverage (public or private) and price of health services.[26] The latest review of lung transplantation reported costs between USD 42,459 and USD 154,051 per quality-adjusted life year.[26] In the present study, median costs (not including the costs for donor acquisition and labor) for the index hospitalization were USD 108,286, approximately matching the cost in the United States.[9,27] However, readmission costs for all recipients who were discharged after transplantation are not well known, although a part of these is covered by Medicare.[28] Our study clarified the costs for index admission as well as readmission costs in Japan.

In comparison with CLT, LDLLT may show several advantages associated with its lower costs. Some studies have suggested that transplant surgery outside regular working hours and donor acquisition in a remote area incur high expenses.[29,30] However, LDLLT is scheduled during regular working hours, and the donor's lungs come from an operating room next door, with no time lag. Therefore, the cost of the index hospitalization is likely to be lower in LDLLT, despite the higher rate of extracorporeal membrane oxygenation use.[5] Moreover, the cumulative number of readmissions may have mainly been reflected in the costs; thus, medical costs may have been lower in LDLLT as a result of fewer readmissions. We observed no readmission to the ICU requiring reintubation or repeat operation in the first year after discharge. Furthermore, because the rate of development of pneumonia or bronchiolitis obliterans did not show a significant difference between the 2 groups, the length of hospital stay owing to these factors was considered to not have had a large effect on the difference in costs.

Limitations

First, this was a retrospective study using an administrative database prone to unmeasured confounders such as socioeconomic status. Second, information on medical resources associated with donor acquisition and outpatient data was lacking in the database. Specific details regarding the costs associated with LDLLT donor surgery and readmission were also unavailable. Furthermore, information on procedures that are not covered by medical insurance, such as nitric oxide inhalation, may not be precise owing to the nature of the database. The database could not differentiate between different techniques such as CPB and ECMO. Third, we were unable to evaluate the lung allocation scores because a scoring system has not yet been established in Japan. In general, LDLLT recipients are highly selected because their donor candidates include only immediate family members including blood-related relatives within the third degree or a spouse. However, LDLLT is often performed for recipients with rapidly deteriorating respiratory function.[3] Thus, the lung allocation score would be higher in LDLLT. Fourth, the rates of readmission and mortality may be underestimated because hospitalizations in facilities other than those for transplantation could not be followed up, and deaths outside the hospitals were not captured. However, patients in Japan are likely to be treated at the same transplant centers in most cases, and patients with LDLLT and CLT are likely to be affected in the same manner. Furthermore, it is generally assumed that recipients in Japan have their deaths confirmed within the hospital, making deaths occurring outside the hospital extremely rare. Finally, there may exist a center bias in the rates of lung transplants performed. Among the 9 facilities, approximately 80% of the LDLLT was performed at 2 facilities. However, these facilities also had a higher proportion of CLT procedures. This suggested a low influence of center bias on the readmission policy between the 2 groups.

Conclusions

LDLLT showed a reduced risk for acute care service utilization associated with postdischarge readmissions. The readmission rate and total cost at 90 days after discharge were significantly lower with LDLLT, with similar trends without significance observed 1 year after discharge. Further studies with larger cohorts are needed to confirm the long-term benefits.

CRediT authorship contribution statement

Conception and design of the study: N.Y., T.J., M.S., T.N., and J.N. Data acquisition: N.Y., T.J., R.K., H.M., K.F., and H.Y. Statistical analysis: N.Y., T.J., H.M., K.F., and H.Y. Interpretation of data: all authors. Manuscript drafting: N.Y., T.J., M.S., and H.Y. Critical revision for important intellectual content and final approval of the submitted draft: all authors.

Disclosure statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Hideo Yasunaga reports a relationship with The Ministry of Health, Labour and Welfare, Japan (21AA2007 and 22AA2003) and the Ministry of Education, Culture, Sports, Science and Technology, Japan (20H03907) that includes funding grants.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2023.100010.

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